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*J Anim Sci* 2001. 79:2679-2687.

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# Influence of feeding level during postweaning growth on circulating concentrations of thyroid hormones and extrathyroidal 5'-deiodination in steers<sup>1</sup>

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**ABSTRACT:** An experiment was conducted with 42 growing Montbéliard steers to study the effect of feed restriction, followed by refeeding, on circulating concentrations of thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>) and on hepatic and muscle activities of 5'-deiodinase (5'D). At 9 mo of age, 21 steers were diet-restricted for 3 mo (ADG, 641 g/d), prior to a 4-mo compensatory growth period with ad libitum access to the same diet (ADG, 1,240 g/d). They were compared to 21 control steers continuously gaining 1,100 g/d between 9 and 16 mo of age. Blood samples were collected every 14 d and samples of liver and semitendinosus and triceps brachii (triceps) muscles were obtained at slaughter at the end of the restriction and refeeding periods (12 and 16 mo of age, respectively). Compared to control steers, feed restriction decreased plasma concentrations of T<sub>4</sub> after 56 to 83 d of feed restriction ( $P < 0.05$ ), whereas T<sub>3</sub> concentration decreased only after 83 d of feed restriction ( $P < 0.05$ ). No differences in hepatic and muscle 5'D activities were observed after 87 d of feed restriction

and decreased growth rate (12 mo of age). During the refeeding period (compensatory growth), circulating concentrations of T<sub>4</sub> and T<sub>3</sub> were restored to control levels within 14 d. Moreover, T<sub>3</sub> concentration rose above that of control steers after 56 d of refeeding and remained higher for the duration of the experiment ( $P < 0.05$ ). Hepatic 5'D activity was higher ( $P = 0.07$ ) in compensated than in control steers at the end of refeeding period (16 mo of age) and higher ( $P < 0.01$ ) after compensation at 16 mo than during restriction at 12 mo. Activities of 5'D in semitendinosus and triceps muscles were higher ( $P < 0.001$ ) in 16-mo-old than in 12-mo-old steers, but no differences were observed due to feed restriction or compensatory growth. These results indicate that nutritional status regulates both thyroidal secretion and extrathyroidal T<sub>3</sub> production in cattle. The data also suggest that extrathyroidal T<sub>3</sub> production may be involved in the mechanism of compensatory growth in cattle.

Key Words: Cattle, Compensatory Growth, Deiodination, Restricted Feeding, Thyroxine, Triiodothyronine

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J. Anim. Sci. 2001. 79:2679–2687

## Introduction

The increased rate of gain in cattle undergoing a realimentation period after a restricted feeding period is commonly referred to as compensatory growth and is generally practiced during extensive rearing of beef cattle. Many biological factors may account for compensatory growth, such as changes in feed intake, effi-

ciency of energy and protein utilization, maintenance energy, and composition of gain (Carstens et al., 1989; Hicks et al., 1990). Dietary intake and energy modifications are known to affect the thyroid status of growing mammals (Eales, 1988), including cattle (Blum et al., 1985). Thyroid status, as evaluated by circulating concentrations of thyroid hormones, is compromised during dietary energy restriction in steers (Blum et al., 1985) and bulls (Janan et al., 1995) but it returns to normal after refeeding associated with compensatory growth. It has been suggested (Janan et al., 1995) that these changes in thyroid status are controlled by thyroidal secretion and extrathyroidal metabolism of thyroid hormones, but no direct data are available in cattle to support this hypothesis. Whereas the prohormone thyroxine (T<sub>4</sub>) is produced only in the thyroid, the most metabolically active thyroid hormone, triiodothyronine (T<sub>3</sub>), is mainly generated in extrathy-

<sup>1</sup>We thank Rt. Jailler and his team for animal management and blood sampling, Rd. Jailler and his team for animal slaughter, Rd. Jailler for statistical analysis of animal performances, and G. Gentès and J. L. Montel for excellent technical assistance. We are particularly grateful to Y. Geay and J. F. Hocquette for helpful discussions.

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Received December 7, 2000.

Accepted May 25, 2001.

**Table 1.** Composition of experimental diets during the restricted feeding and refeeding periods<sup>a</sup>

Ingredient, kg DM/d	Dietary restriction		Refeeding	
	Control	Restricted	Control	Refed
Corn silage	5.373	4.232	5.914	6.551
Whole shelled corn	1.227	0.439	1.903	1.974
Soybean meal	0.418	0.599	0.140	0.347
Urea	0.061	0.013	0.117	0.114
Dry matter intake	7.079	5.283	8.074	8.986

<sup>a</sup>During the restriction period (from 9 to 12 mo of age), feed intakes were programmed for ADG of 1,200 and 600 g/d for control and restricted steers, respectively. Refed steers (from 12 to 16 mo of age) had ad libitum access to feed.

roidal tissues by enzymatic 5'-deiodination of T<sub>4</sub>. The extrathyroidal activity of 5'-deiodinase (5'D) is an important control point for regulating the thyroid status of tissues in various physiological and pathological situations (Kaplan, 1986).

The main objective of the present study was to evaluate the effect of food restriction and refeeding associated with reduced and compensatory growth, respectively, on circulating concentrations of thyroid hormones and activity of type-I 5'D in liver and muscle of Montbéliard steers. In addition, we investigated the evolution of circulating concentrations of thyroid hormones in preruminant, weaned, and growing Montbéliard steers during continuous growth.

## Materials and Methods

### General Experimental Protocol

This study included 42 Montbéliard calves of comparable chronological age reared at the experimental domain of the National Institute for Agricultural Research (INRA, Institut National de la Recherche Agronomique) in Clermont-Ferrand-Theix, France. The study was carried out as part of a research program approved by the INRA Ethical Committee. At 2 mo of age (105 kg), the calves were surgically castrated. Up to 2 mo of age, they received an artificial milk diet (Univor energie; Centraliment, Aurillac, France). Milk intakes were gradually decreased until 4 mo of age, when the steers were only fed a diet consisting of corn silage, concentrates, and hay. The diet was formulated on the basis of live weight (INRA, 1988). Average daily gains were 1,047 and 1,100 g/d during the milk and postweaning periods, respectively. At 9 mo of age, the steers were randomly assigned to either a standard feed ration (control group, *n* = 21) or feed restriction for 87 d (restricted group, *n* = 21). Control steers were offered an amount of diet to ensure a daily weight gain of 1,200 g (Table 1). The restricted group was limit-fed the same diet from 9 to 12 mo of age. Feed restriction consisted of a 24.5% energy restriction and of a 22.5% protein restriction and was designed to decrease the ADG to 60% of that in control steers. At the end of

the restriction period (12 mo of age), 10 animals per treatment combination were slaughtered. The remaining steers in the restricted group were then allowed ad libitum access to feed (restricted-refed group, *n* = 11) and the remaining control animals (*n* = 11) received the same diet to ensure continuous growth with ADG of 1,200 g/d (Table 1). We chose ad libitum access to feed for steers in the refed group in order to emphasize the magnitude of compensatory growth. After 4 mo of realimentation all steers were slaughtered at 16 mo of age.

During the experimental period, individual live body weights were recorded weekly, and weights on two consecutive days were recorded at 2-wk intervals. Steers were housed indoors and were provided with water continuously. From 8 to 12 mo of age, all steers were individually penned (1.8 m<sup>2</sup> per steer) and were individually fed to control feed intake. From 12 to 16 mo of age, the two groups were managed in loose housing (6.5 m<sup>2</sup> per steer). Steers were slaughtered at the experimental facility of the INRA Research Center Clermont-Ferrand/Theix, France in compliance with ethical guidelines for animal care. Liver and muscle samples from semitendinosus and triceps brachii (triceps) were collected from the right side of the carcass within 15 min after exsanguination, snap-frozen in liquid nitrogen, and stored at -80°C until they were analyzed.

### Hormone Determinations

For analysis of the influence of age on concentrations of thyroid hormones, blood samples were collected by venipuncture from the jugular vein of 10 control steers at 15 d and at 4, 8, 12, and 16 mo of age. For the analysis of the influence of the feeding level on concentrations of thyroid hormones during postweaning growth, blood was collected every 14 d during the restriction (*n* = 10) and refeeding (*n* = 11) periods. The remaining feed was removed the night before blood collection but steers had free access to water. Blood samples from the jugular vein were collected on potassium-EDTA (1.6 mg/mL) and Antagosan (5 U/mL). The plasmas were separated by centrifugation within

15 min and kept frozen at  $-20^{\circ}\text{C}$  until analysis. Concentrations of total  $\text{T}_4$  and  $\text{T}_3$  were determined in duplicate by radioimmunoassay using commercial kits (AM-ERLEX-M, Ortho Clinical Diagnostics France). Lower limits of sensitivity were 3 ng/mL for  $\text{T}_4$  and 0.1 ng/mL for  $\text{T}_3$ . For each period, samples from both groups were analyzed in the same assay. Intraassay coefficients of variation were 3.3% for  $\text{T}_4$  and 3.7% for  $\text{T}_3$ . Hormone concentrations are presented as mean values with their SE.

#### *5'-Deiodinase Determination (Type-I)*

5'-Deiodinase activity was determined in liver and muscle samples collected at slaughter from control and feed-restricted steers at 12 mo ( $n = 10$ ) and from control and refed steers at 16 mo ( $n = 11$ ) of age. Outer-ring deiodinating activity (5'D) was determined by quantifying the  $^{125}\text{I}^-$  released from 3,3',5'-[ $^{125}\text{I}$ ] $\text{T}_3$  ( $\text{rT}_3$ ) as previously described (Kahl et al., 1995). In brief, samples of liver and muscle were homogenized in 0.01 M HEPES buffer (pH 7.0, 0.25 M sucrose, 5 mM EDTA) using a Polytron homogenizer (Brinkman Instruments, Westbury, NY). After centrifugation (30 min at  $2,000 \times g$ ), the supernate was incubated for 5 min (liver) or 60 min (muscle) in 0.1 M phosphate buffer (pH 7.0, 1 mM EDTA) in the presence of 5 mM (liver) or 20 mM (muscle) dithiothreitol at  $37^{\circ}\text{C}$  with approximately 80,000 cpm of [ $^{125}\text{I}$ ] $\text{rT}_3$  (DuPont-New England Nuclear, Boston, MA) and 1  $\mu\text{M}$  (liver) or 20 nM (muscle) of unlabeled  $\text{rT}_3$  (Calbiochem, La Jolla, CA). The assay mixture contained 30 to 50  $\mu\text{g}$  (liver) or 120 to 200  $\mu\text{g}$  (muscle) of protein. The released  $^{125}\text{I}^-$  was isolated as trichloroacetic acid (TCA)-soluble radioactivity. The 5'D activity was expressed as nanomoles (liver) or femtomoles (muscle) of  $\text{I}^-$  per hour per milligram of protein. Protein concentration in homogenates was determined with bicinchoninic acid reagent and BSA as a standard (Pierce Chemical, Rockford, IL).

#### *Statistical Analysis*

Live body weights and thyroid hormone concentrations were analyzed for each nutritional period using the MIXED procedure (SAS Inst. Inc., Cary, NC; Littell et al., 1998), based on the assumption that repeated observations on the same steer are likely related. Data were analyzed in a model that contained the fixed effects: period of nutrition (restriction or refeeding); group and time, both tested within the period of nutrition; and the period of nutrition  $\times$  time interaction. Time was considered repeated on the same steer, which was nested within the period of nutrition and group. When significant effects were detected, differences between means were further separated by the PDIF option of SAS.

Analysis of variance (Steel and Torrie, 1980) of growth parameters and 5'D activities was made using the GLM procedure of SAS (SAS Inst. Inc.). For hepatic

5'D activity, the effects tested in the model included period of nutrition (restriction or refeeding) and group tested within the period of nutrition. For muscle 5'D activities, the effects tested in the model included period of nutrition (restriction or refeeding); group tested within the period of nutrition; steer tested within the period of nutrition and group; muscle; and period of nutrition  $\times$  muscle and group  $\times$  muscle interactions. The period of nutrition and group factors were tested against steers within the period of nutrition and group. The residual mean square was used as the error term for other effects. When significant effects were detected, differences between means were further separated by the PDIF option of SAS.

## **Results**

### *Plasma Concentrations of Thyroid Hormones During the Growth Periods of Steers*

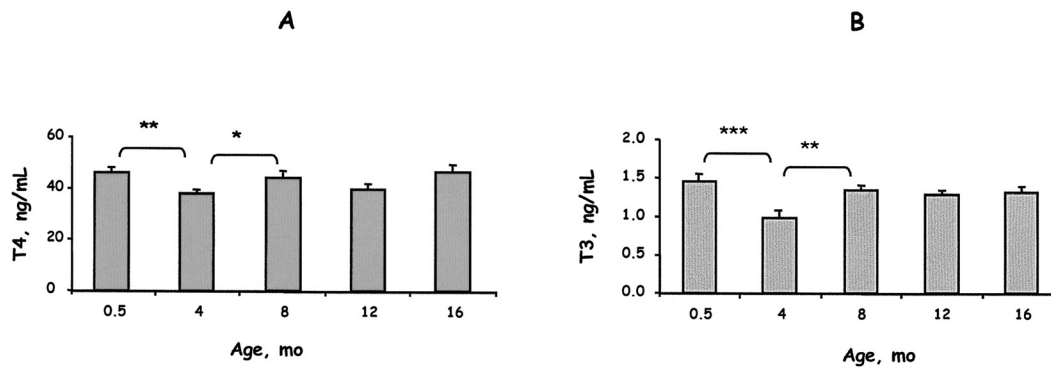
Plasma concentrations of  $\text{T}_4$  and  $\text{T}_3$  during continuous growth of 10 control Montbéliard steers between 15 d and 16 mo of age are presented in Figure 1. Mean total plasma concentrations of  $\text{T}_4$  and  $\text{T}_3$  during that time were, respectively, 45 and 1.45 ng/mL. By the end of the weaning period (4 mo) concentrations of  $\text{T}_4$  and  $\text{T}_3$  were at their nadir;  $\text{T}_4$  and  $\text{T}_3$  were decreased, respectively, 17.5 ( $P < 0.01$ ) and 32% ( $P < 0.001$ ) compared to milk-fed calves at 15 d and 14 ( $P < 0.05$ ) and 27% ( $P < 0.01$ ) compared to 8-mo-old weaned calves.

### *Growth Performance of Steers During the Restriction and Refeeding Periods*

The performance of growing steers during the periods of restriction and refeeding is presented in Figure 2. The 3 mo of dietary restriction imposed on the steers resulted in a 39% reduction in ADG compared to control steers (641 vs 1,049 g/d, SEM = 52 g/d,  $P < 0.001$ ). Live BW was lower in restricted than in control steers from d 42 of restriction onward ( $P < 0.05$ ). On d 87 of restriction, BW was 37 kg lower for restricted than for control steers (382 vs 419 kg, SEM = 6 kg,  $P < 0.001$ ). Refeeding of the restricted steers resulted in compensatory growth with higher ADG than for control animals (1,240 vs 1,089 g/d, SEM = 49 g/d,  $P < 0.05$ ). Compensatory growth was observed during the 42 d following refeeding. From d 42 of compensation onward, the BW of control steers and steers experiencing compensatory growth did not differ significantly. On d 128 of refeeding, BW in control and refed steers were 552 and 542 kg (SEM = 11 kg), respectively.

### *Plasma Concentrations of Thyroid Hormones in Steers Undergoing Compensatory Growth After Feed Restriction*

The effects of dietary restriction and refeeding on plasma concentrations of total  $\text{T}_4$  and  $\text{T}_3$  are presented

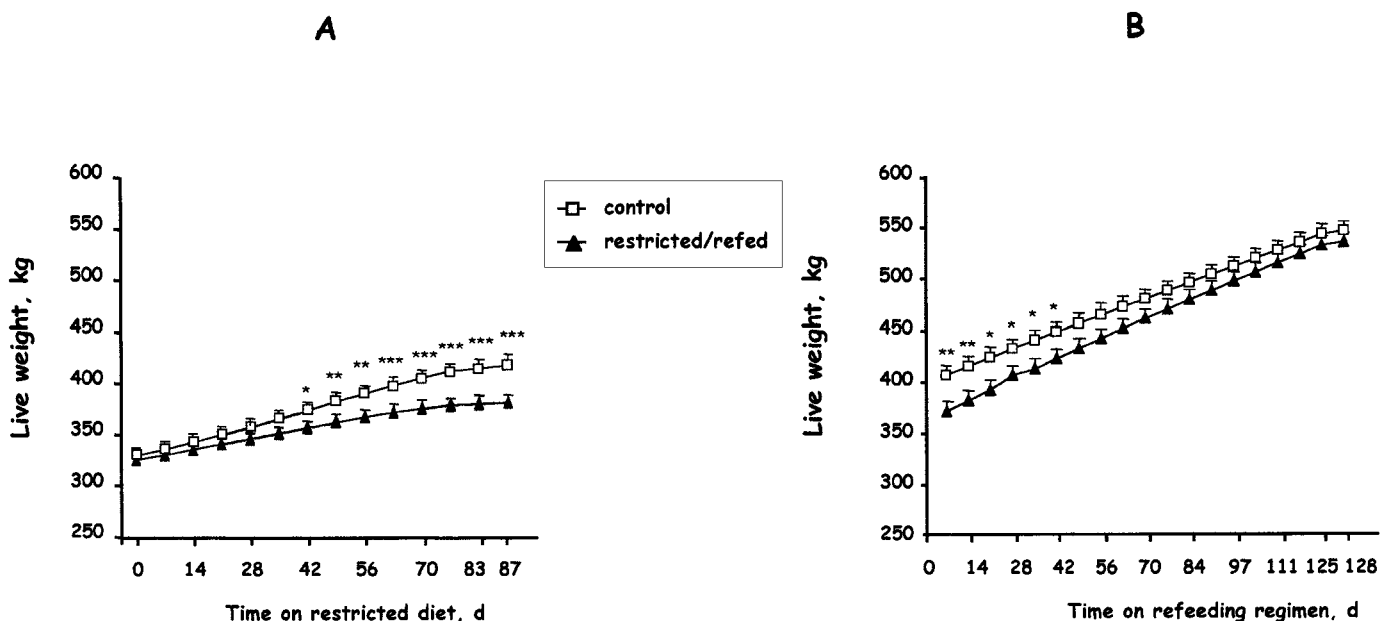


**Figure 1.** Plasma concentrations of thyroid hormones during continuous growth of 10 control Montbéliard steers. (A) Thyroxine (T<sub>4</sub>); (B) triiodothyronine (T<sub>3</sub>). \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  between age groups.

in Figures 3 and 4. For the restriction period, there was a highly significant interaction between time and nutrition for T<sub>4</sub> ( $P < 0.001$ ) but not for T<sub>3</sub> ( $P = 0.18$ ). Circulating concentrations of T<sub>4</sub> (Figure 3A) transiently decreased in restricted steers at the beginning of the restriction period (d 14 vs d 28) and remained unaltered until d 42. At the end of the restriction period, a marked decrease was observed in both restricted ( $P < 0.001$ ) and control ( $P < 0.01$ ) animals (d 70 vs d 83). Compared to control steers, plasma T<sub>4</sub> concentrations were lower in restricted steers on d 56 (−13%,  $P < 0.05$ ), and d 83 (−17%,  $P < 0.05$ ). Plasma T<sub>3</sub> concentrations (Figure 3B) decreased in restricted steers between d 14 and d 28 ( $P < 0.001$ ), remained unchanged until d 70, and decreased again between d 70 and d 83 ( $P < 0.01$ ). However, T<sub>3</sub> concentrations

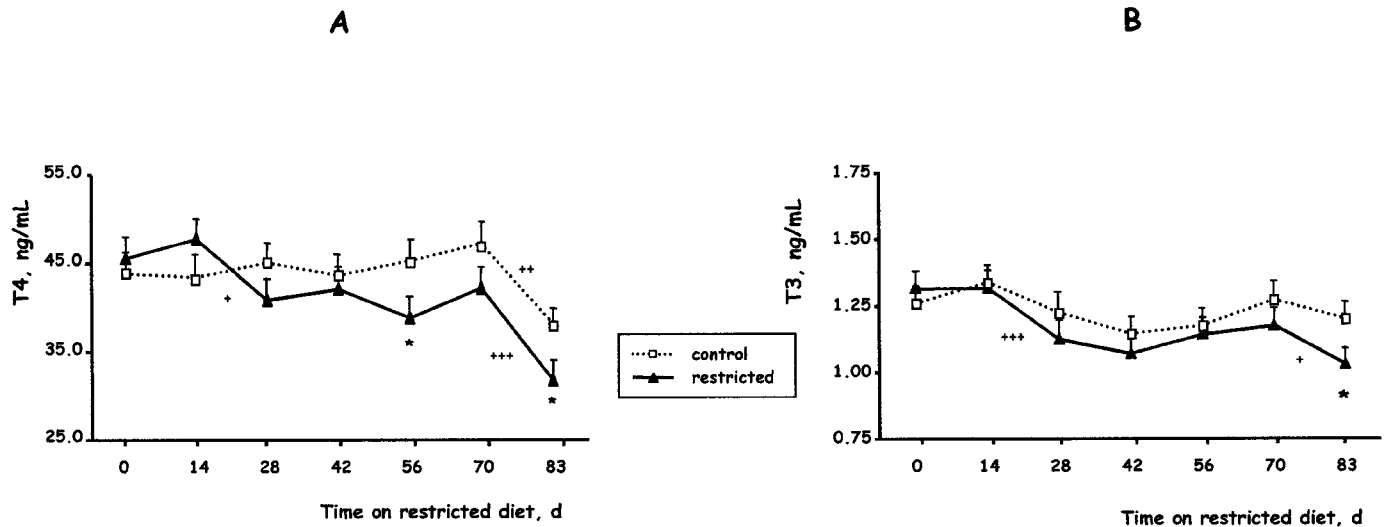
were not different between control and restricted steers until d 83 of the restriction period (16% lower in restricted than control,  $P < 0.05$ ).

For the refeeding period, there was a significant interaction between time and nutrition for T<sub>4</sub> ( $P < 0.001$ ) and T<sub>3</sub> ( $P < 0.01$ ). Differences in the mean plasma concentrations of total T<sub>4</sub> and T<sub>3</sub> at the end of the feed restriction period disappeared within the first 14 d of refeeding (Figure 4), when plasma concentrations of both hormones markedly increased ( $P < 0.001$ ) in steers experiencing compensatory growth. Thereafter, no differences in plasma T<sub>4</sub> concentrations were observed between control and refeed steers, except at d 70 ( $P < 0.05$ ). Following the initial elevation, T<sub>3</sub> concentrations fell between d 28 and 42 (−30,  $P < 0.001$ ) in the restricted-reallocated steers, but also in the



**Figure 2.** Live body weight gain of control and restricted-refed steers. (A) Restriction period (n = 21); (B) refeeding period (n = 11). During the restriction period, feed intakes were programmed for ADG of 1,200 and 600 g/d for control and restricted steers, respectively. Refed steers had ad libitum access to feed. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$  between treatment groups at specific times.



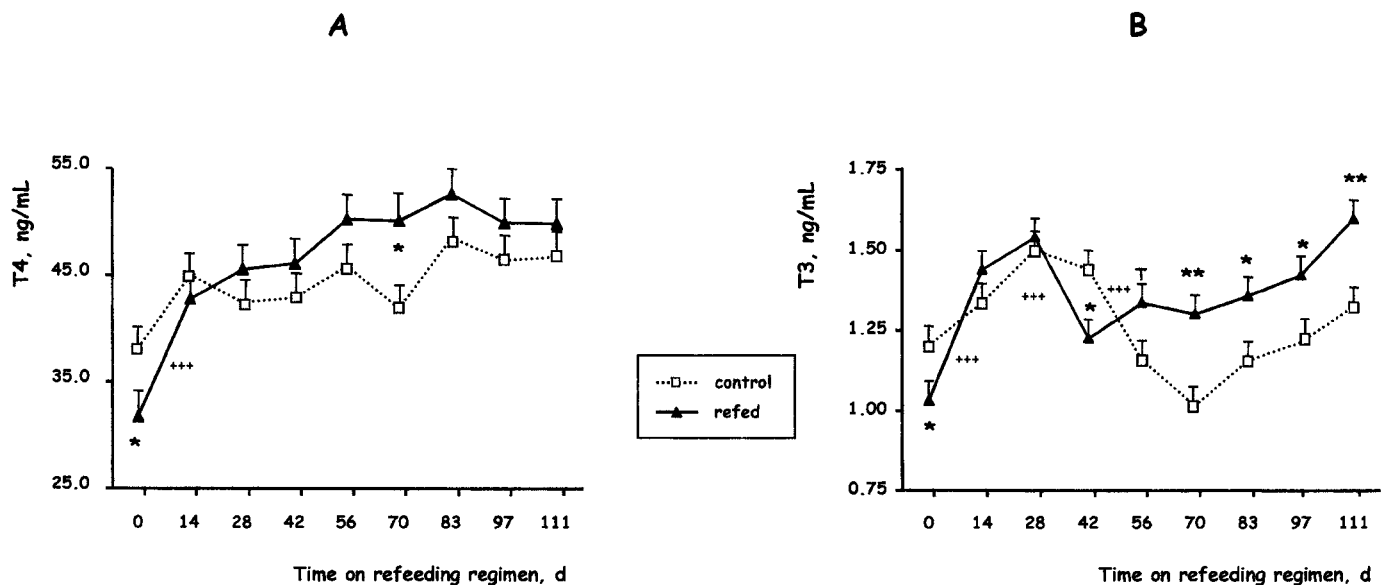


**Figure 3.** Effects of dietary restriction on plasma concentrations of thyroid hormones. (A) Thyroxine (T<sub>4</sub>); (B) triiodothyronine (T<sub>3</sub>). During the restriction period, feed intakes were programmed for ADG of 1,200 and 600 g/d for control and restricted steers, respectively. \* $P < 0.05$  between control and restricted group and + $P < 0.05$ , ++ $P < 0.01$ , +++ $P < 0.001$  between two consecutive blood samplings in the same group.

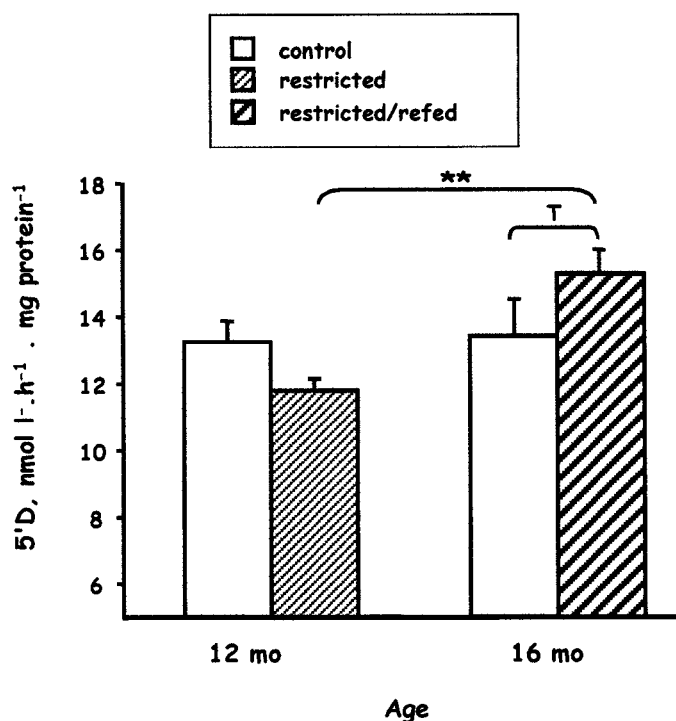
control group between d 42 and 56 ( $-20\%$ ,  $P < 0.001$ ). However, T<sub>3</sub> concentrations were always higher in steers experiencing compensatory growth than in control steers between d 56 of refeeding and the end of the experiment ( $P < 0.05$ ). At the end of the refeeding period (d 111), plasma T<sub>3</sub> concentrations were 21% higher for restricted-refed than for control steers ( $P < 0.01$ ).

#### *Hepatic and Muscle 5'-Deiodinase Activity in Steers at the End of the Feed Restriction and Refeeding Periods*

Hepatic 5'D activities are shown in Figure 5. Feed restriction for 3 mo did not significantly affect activity of type-I 5'D in liver ( $P = 0.19$ ). However, numerically, lower values ( $-11.8\%$ ) were observed for feed-re-



**Figure 4.** Effects of ad libitum access to feed following feed restriction on plasma concentrations of thyroid hormones in steers. (A) Thyroxine (T<sub>4</sub>); (B) triiodothyronine (T<sub>3</sub>). During this experimental period, previously feed-restricted steers were allowed ad libitum access to feed. Control steers received the amount of the same diet to ensure ADG of 1,200 g/d. <sup>T</sup> $P < 0.1$ , \* $P < 0.05$ , \*\* $P < 0.01$  between control and restricted-refed group and +++ $P < 0.001$  between two consecutive blood samplings in the restricted-refed group.



**Figure 5.** Effects of dietary restriction and refeeding on hepatic thyroxine 5'-deiodinase (5'D) activity. During the restriction period (from 9 to 12 mo of age), feed intakes were programmed for ADG of 1,200 and 600 g/d for control and restricted steers, respectively. Refed steers (from 12 to 16 mo of age) had ad libitum access to feed. <sup>T</sup> $P = 0.07$  between control and restricted-refed group at 16 mo of age and  $**P < 0.01$  between restricted group at 12 mo and restricted-refed group at 16 mo of age.

stricted than for control steers at 12 mo of age. At the end of the refeeding period (16 mo of age) hepatic activities of 5'D tended to be 14.1% higher ( $P = 0.07$ ) in steers undergoing compensatory growth than in control animals. For restricted-refed steers, hepatic 5'D activity was higher ( $P < 0.01$ ) at the end of the compensatory growth period (16 mo of age) than at the end of the feed restriction period (12 mo of age). Activities of 5'D in muscle tissue are presented in Figure 6. On the basis of protein concentration, the average 5'D activity in muscle tissue was less than 0.01% of the activity in liver. Interestingly, it was higher in the triceps than in the semitendinosus muscle ( $P < 0.01$ ). Feed restriction or refeeding did not significantly affect 5'D activities in either muscle. However, in both muscles the values were significantly higher ( $P < 0.001$ ) in 16-mo-old than in 12-mo-old steers.

## Discussion

### *Influence of Weaning on Circulating Concentrations of Thyroid Hormones*

Plasma concentrations of thyroid hormones were relatively stable in normally growing steers during the

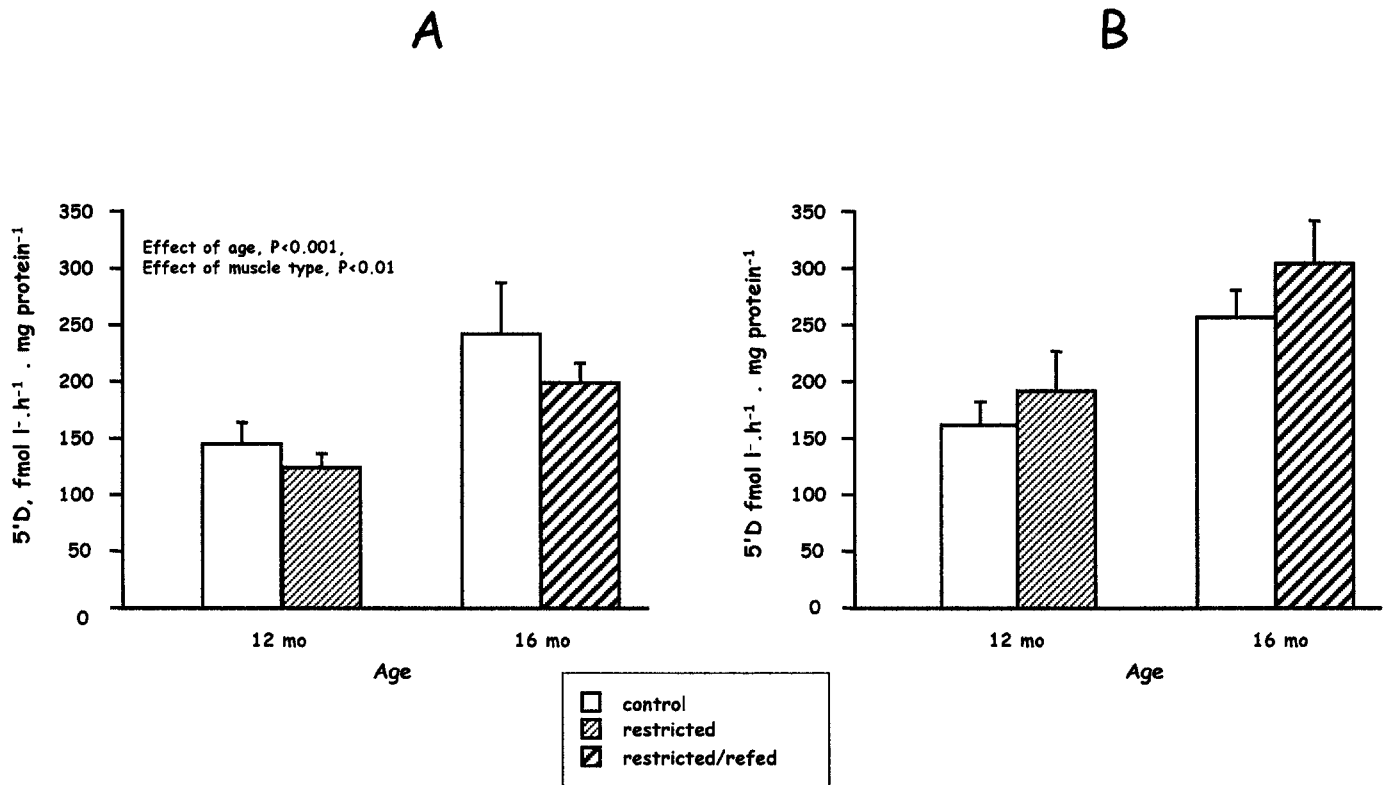
first 16 mo of life, with the exception of a marked decrease observed by the end of the weaning period (4 mo of age). This finding could be expected, because weaning is a critical phase in ruminant development and is characterized by functional and metabolic changes in digestive processes. In particular, marked changes in nutrient balance occur during the suckling-weaning transition: fat and carbohydrate provided by milk replacer decrease and volatile fatty acids become the major end-products of digestion. Moreover, the change from a liquid to a solid diet requires an adaptation of digestive physiology. Thus, the period around weaning corresponds to a transient undernutrition, as shown by the decrease in ADG (data not shown). Bovine thyroidal status is known to be affected by energy availability (Blum et al., 1985; Janan et al., 1995) and by nutrients such as glucose or fatty acids (Ahn and Rosenberg, 1980; Romo et al., 1997). Therefore, energy restriction associated with changes in the diet (weaning, corn-silage transition period) may be responsible for the decreases in circulating concentrations of  $T_4$  and  $T_3$  by the age of 4 mo.

### *Influence of Feeding Level in the Postweaning Growth Period on Thyroidal Status*

Plasma concentrations of thyroid hormones were altered in relation to feed intakes and growth rate in growing steers, as previously reported (Blum et al., 1985; Pethes et al., 1985; Ellenberger et al.). Restricted feeding for 87 d (to reduce the ADG to 60% of control values) resulted in decreased BW growth evident from d 42 onward. Plasma thyroid hormone concentrations responded to feed restriction, as previously described for steers (Blum and Kuntz, 1981; Blum et al., 1985; Janan et al., 1995) and sheep (Blum et al., 1980). In the present experiment, both plasma  $T_4$  and  $T_3$  decreased sharply between d 14 and 28 of restriction. However, compared to concentrations in control steers,  $T_4$  concentrations were reduced ( $P < 0.05$ ) in restricted steers after 56 d of restriction and  $T_3$  concentrations decreased only at the end of the restriction period (d 83). These data indicate that feed restriction in steers decreased thyroidal secretion rather than extrathyroidal  $T_3$  generation. They also support previous studies that indicate circulating  $T_4$  is more closely associated with energy consumption than is circulating  $T_3$  (Elsasser et al., 1989; Hayden et al., 1993).

Realimentation reversed the effects of restricted feed intake. Compensatory body growth was apparent after d 42 of refeeding. As previously shown (Hayden et al., 1993; Yambayamba et al., 1996; Barash et al., 1998), plasma thyroid hormone concentrations rapidly increased in response to refeeding. In our experiment, they were restored to control levels within 14 d (Figure 4).

As expected, changes in plasma concentrations of thyroid hormones were associated with shifts in energy and protein intake. Previously, plasma  $T_4$  concen-



**Figure 6.** Effects of dietary restriction and refeeding on muscle thyroxine 5'-deiodinase (5'D) activity. (A) Semitendinosus; (B) *triceps brachii*. During the restriction period (from 9 to 12 mo of age), feed intakes were programmed for ADG of 1,200 and 600 g/d for control and restricted steers, respectively. Refed steers (from 12 to 16 mo of age) had ad libitum access to feed.

tration was found to be an indicator of energy balance, BW gain, and protein deposition (Ellenberger et al., 1989; Hayden et al., 1993). Also, a positive correlation has been demonstrated between  $T_4$  concentration and growth rate in cattle (Graf and Grosser, 1979). Moreover, circulating  $T_3$  concentrations in steers were shown to change in parallel with the intake of metabolizable energy (Blum et al., 1979). The interesting finding in the present study was that the time courses of  $T_4$  and  $T_3$  variations were different during the restriction and compensation periods. First, plasma  $T_3$  concentrations responded to dietary restriction more slowly than did  $T_4$  concentrations. This finding was in accordance with the report by Ellenberger et al. (1989) of unchanged  $T_3$  concentrations in spite of decreased  $T_4$  concentrations in steers fed 50% of ad libitum consumption. Triiodothyronine is the most metabolically active thyroid hormone (Larsen et al., 1981), whereas  $T_4$ , the main secretory product of the thyroid gland and the most abundant iodothyronine in the circulation, has little, if any, biological activity (Surks and Oppenheimer, 1977). Therefore, maintaining normal circulating concentrations of  $T_3$  during a period of limited nutrient availability could be metabolically desirable for growing steers. Second,  $T_3$  concentrations were increased during the realimentation period, whereas accompanying changes in  $T_4$  concentrations

were less apparent. A similar observation was reported in Holstein-Friesian bulls during refeeding after severe energy restriction (Janan et al., 1995). Interestingly, the growth rate of Holstein calves was better correlated with circulating concentrations of  $T_3$  than of  $T_4$  (Kahl and Bitman, 1983). It has been also suggested that  $T_3$  could be the only thyroid hormone required to maintain normal and Synovex-S-stimulated growth and protein accretion in beef steers (Kahl et al., 1992). According to Gerrits et al. (1998),  $T_3$  may be involved in the response of protein deposition to increased fat and carbohydrate energy intakes in pre-ruminant calves. Therefore, increased circulating concentrations of  $T_3$  during the refeeding period in our experiment suggests that the active form of thyroid hormone ( $T_3$ ) may participate in the mechanism of compensatory gain.

Triiodothyronine is produced by enzymatic deiodination of  $T_4$  within the thyroid gland and peripheral tissues. In euthyroid animals, extrathyroidal  $T_4$  to  $T_3$  conversion, especially in the liver, is responsible for most of the circulating  $T_3$  (Leonard and Visser, 1986). Plasma  $T_4$  concentration is a result of the balance between thyroidal secretion and peripheral metabolism (affinity for carrier proteins, deiodination, catabolism, clearance). The activity of extrathyroidal 5'D plays an important role in the regulation of ruminant thyroid



status in various physiological or pathological situations (Kahl et al., 1984, 1998). In the present experiment, restricted feeding did not affect activity of type-I 5'D in liver and muscle. These data indicate that, in spite of a reduction in thyroidal secretion and subsequent decrease in plasma  $T_4$  concentration during the restricted-feeding period, extrathyroidal 5'D activities remained sufficient to compensate for the depressed thyroidal activity in maintaining normal concentrations of circulating  $T_3$ . However, the decrease in plasma  $T_3$  concentration observed at the end of the restriction period may be due to reduced availability of  $T_4$ , the substrate for  $T_3$  formation.

The substantial increase in plasma concentrations of  $T_3$  accompanied by normal plasma  $T_4$  during the realimentation period in steers experiencing compensatory growth seemed to be associated with the higher activities of hepatic 5'D at the end of the refeeding period. Moreover, the highly significant difference in hepatic 5'D activity between restricted steers at 12 mo and compensated ones at 16 mo indicates that when animals were switched from restricted intake to ad libitum amounts of intake and increased their growth rate, they also increased extrathyroidal production of  $T_3$ , and consequently circulating  $T_3$  concentration. Elevated plasma  $T_3$  concentrations observed in the present experiment during realimentation may also be related to a rebound secretory response of thyroid activity associated with the removal of a condition that otherwise suppresses thyroid secretion during nutrient restriction. Transient increases to supranormal concentrations of circulating  $T_3$ , but not  $T_4$ , have been reported previously in rats (Cooper et al., 1983) and heifers (Thrft et al., 1999) with an experimentally induced hypothyroid state (propylthiouracil) after the discontinuation of antithyroid treatment.

The activities of type-I 5'D in triceps brachii and semitendinosus muscles were not affected by realimentation and compensatory growth. However, the low specific activity (on a protein basis) of muscle 5'D compared to liver 5'D indicates that the total amount of  $T_3$  generated in muscle tissue could supply less than 1% of  $T_3$  produced by the whole liver. Previous studies in rats (Chopra, 1977; Tsukahara et al., 1989) and cattle (Kahl et al., 1984) have shown that activity of 5'D in skeletal muscle is several orders of magnitude lower than in the liver. Therefore, even with the large total mass of muscle tissue in the animal's body, the contribution of muscle 5'D to circulating  $T_3$  seems to be insignificant. Nevertheless, the importance of  $T_3$  produced within the muscle for local needs cannot be excluded. In the present experiment, activities of 5'D were higher in the more oxidative muscle (triceps). Moreover, in both muscles they were higher in 16-mo-old than in 12-mo-old steers. Our unpublished data from the same experiment indicate an increased oxidative metabolism in muscles (citrate synthase, cytochrome oxidase, and isocitrate dehydrogenase), particularly in the triceps muscle, at 16 mo of age. Cyto-

chrome oxidase expression and activity are known to be regulated by  $T_3$  (Wiesner et al., 1992; Paradies et al., 1994). Therefore, coincidental increases in muscle oxidative activities and the potential to produce  $T_3$  in situ suggest that muscle 5'D activity might be important for regulating local metabolic processes in oxidative muscle.

In conclusion, the results of the present study indicate that nutritional status regulates both thyroidal secretion and extrathyroidal production of  $T_3$  in cattle. Hepatic activity of type-I 5'D may be involved in the optimization of circulating concentrations of  $T_3$  to maintain the euthyroid state during feed restriction or to supply increased amounts of  $T_3$  during the realimentation associated with compensatory growth.

## Implications

The present study emphasizes the importance of feeding level in the regulation of thyroid status of growing steers. The response of circulating thyroid hormones to modifications of feeding level involves changes in both thyroid activity and extrathyroidal 5'-deiodination of the prohormone, thyroxine ( $T_4$ ), to metabolically active thyroid hormone, triiodothyronine ( $T_3$ ). Feed restriction for 3 mo resulted in depressed thyroid secretion. However, stable activity of hepatic 5'-deiodinase (5'D) maintained normal concentrations of  $T_3$ . During realimentation, associated with compensatory growth, hepatic 5'D activities increased extrathyroidal production of  $T_3$  and, consequently, circulating concentration of  $T_3$  in spite of normal thyroidal secretion. Therefore, hepatic 5'D activity could be involved in the mechanism of compensatory growth in steers.

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